UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,071	04/05/2006	Maria Gabriella Santoro	2520-1073	7454

466 7590 10/05/2011

YOUNG & THOMPSON
209 Madison Street
Suite 500
Alexandria, VA 22314

EXAMINER	
ZAREK, PAUL E	
ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
10/05/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,071	SANTORO, MARIA GABRIELLA	
	Examiner	Art Unit	
	PAUL ZAREK	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *66,69 and 74-86* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *66,69 and 74-86* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/08/2010 has been entered.

Status of the Claims

2. Claims 66, 69, and 74-78 have been amended, Claims 79-86 have been added, and Claims 65, 67, 68, and 70-73 have been cancelled by the Applicant in correspondence filed on 07/08/2010. Claims 66, 69, and 74-86 are currently pending. This is the first Office Action on the merits of the claim(s) following a request for continued examination.

RESPONSE TO ARGUMENTS

3. Claims 65, 66, 68, 73, 74, 76, and 77 were rejected under 35 U.S.C. 102(b) as being anticipated by Regtop and Biffin (US Patent No. 5,466,824, issued 1995). Claims 65, 68, and 73 have been canceled. Claims 66, 74, and 76 now depend from claim 77, which is drawn to a pharmaceutical composition wherein the active ingredient consists of indomethacin and/or salts thereof, in combination with a pharmaceutically effective amount of at least one metal and/or corresponding salts. Applicant traversed this rejection on the grounds that this prior art does not

anticipate the instant claims. Specifically, Applicant contends that Regtop and Biffin describe a complex of indomethacin, a divalent metal, and a tertiary or cyclic tertiary amide and that the examples disclosed therein are limited to $copper_2indomethacin_4$ complexes. Applicant notes that the purpose of the divalent metal-indomethacin complex is to reduce adverse effects on the gastric mucosa when administered orally. In contrast to the prior art, Applicant argues that the instantly claimed invention is a pharmaceutical composition consisting of a combination of two independent active ingredients: indomethacin and at least one metal. Applicant notes that neither gold nor bismuth exists in a divalent form and that selenium can be divalent or have oxidation states of +6 and +4. Respectfully, Examiner does not find Applicant's argument persuasive.

4. Claim 77 is drawn to a pharmaceutical composition wherein the only active ingredient is the combination of indomethacin and a metal, or salts thereof. Regtop and Biffin disclose compositions comprising indomethacin and a metal, including zinc, cobalt, nickel, and, most preferably, copper. There is no limitation in the claims requiring the indomethacin and metal or metal salt to be non-complexed or that the metal must be a particular metal. Thus, a complex comprising indomethacin and any metal or metal salt reads on the rejected claims. Regtop and Biffin specifically contemplate and prefer copper as a metal to be combined with indomethacin (col 4, ln 19-20). This prior art also exemplifies a pharmaceutical composition comprising indomethacin and copper. Therefore, Regtop and Biffin anticipate all the limitations of the rejected claims.

5. Applicant's arguments regarding the oxidation states of gold, bismuth, or selenium, or the problem the prior art was attempting to solve are irrelevant with respect to the standing anticipation rejection. The prior art discloses each and every limitation of the rejected claims.

Therefore the rejection of Claims 66, 74, 76, and 77 under 35 U.S.C. 102(b) as being anticipated by Regtop and Biffin is maintained.

6. Claims 69 and 70 were rejected under 35 U.S.C. 103(a) as being unpatentable over Regtop and Biffin (above) in view of Berge, et al. (Journal of Pharmaceutical Sciences, 1977). Claim 75 was rejected under 35 U.S.C. 103(a) as being unpatentable over Regtop and Biffin (above) in view of Wilkinson (Goodman & Gilman's The Pharmaceutical Basis of Therapeutics 10th ed., Chapter 1: Pharmacokinetics, 2001). Applicant traversed these rejections on the grounds that the applied prior art does not teach or fairly suggest the instantly claimed invention. Specifically, Applicant argues that Regtop and Biffin do not read on the independent claim 77 for the reasons noted above, and contends that neither Berge, et al., nor Wilkinson compensate for the alleged deficiencies of this prior art. Respectfully, Examiner does not find Applicant's argument persuasive.

7. Regtop and Biffin disclose a composition comprising indomethacin and a metal salt (see above), and thus read on Claim 75. Applicant has not disagreed with Berge, et al., or Wilkinson in the capacity with which they were applied. Therefore, the rejections of Claims 69 and 70 under 35 U.S.C. 103(a) as being unpatentable over Regtop and Biffin in view of Berge, et al., and Claim 75 under 35 U.S.C. 103(a) as being unpatentable over Regtop and Biffin in view of Wilkinson are maintained.

8. Claim 78 was rejected under 35 U.S.C. 103(a) as being unpatentable over Regtop and Biffin (above) in view of Taylor, et al. (US Patent No. 6,303,295, issued 2001). This rejection is withdrawn.

9. Below are listed new grounds of rejection necessitated by the filing of a request for continued examination. Therefore, this office action is considered **non-final.**

Claim Rejections - 35 USC § 112 (2nd paragraph)

10. The text of Title 35, U.S.C. § 112, second paragraph, can be found in a prior Office action.

11. Claims 78, 81, and 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 78, 81, and 84 limit the metal of Claim 77 to be selenium. There is insufficient antecedent basis for this limitation in the claim because selenium is not a metal.

Claim Rejections - 35 USC § 103

12. The text of Title 35, U.S.C. § 103(a) can be found in a prior Office action.

13. Claims 66, 69, and 74-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts and Morrow (Goodman & Gilman's The Pharmacological Basis of Therapeutics, 10th ed., Chapter 27: Analgesic-antipyretic and anti-inflammatory agents and drugs employed in the treatment of gout, 2001), May (Expert Opinion on Investigational Drugs, 1999), Douthwaite (British Medical Journal, 1944), Berge, et al. (Journal of Pharmaceutical Sciences, 1977; already of record), and Wilkinson (Goodman & Gilman's The Pharmaceutical Basis of Therapeutics 10th ed., Chapter 1: Pharmacokinetics, 2001; already of record).

14. Claims 69, 74, 77, and 78 were described previously. Claim 79 limits the pharmaceutical composition of Claim 76 to be selected from among numerous classes of excipients (i.e. solubilizing agents, stabilizing agents, and salts). Claims 80 and 83 limit the metal of Claim 77 to be gold or a gold salt, respectively. Claims 81 and 84 limit the metal of Claim 77 to be selenium or a selenium salt, respectively. Claims 82, 85, and 86 limit the metal of Claim 77 to be bismuth, a bismuth salt, or bismuth chloride, respectively.

15. Roberts and Morrow teach that indomethacin is useful for the treatment of rheumatoid arthritis and can be administered orally (pgs 705-706). This art also teaches that gold and its salts are useful for the treatment of rheumatoid arthritis and can be administered orally (pgs 716-718). May teaches that selenium is effective for treating articular pain and morning stiffness in patients suffering from rheumatoid arthritis (pg 1021, paragraph spanning col 1 and 2). Douthwaite teaches that bismuth is effective for treating rheumatoid arthritis ("Conclusion"). Given that indomethacin and each of the specifically claimed metals are useful for the treatment of rheumatoid arthritis, it would have been *prima facie* obvious to combine them in a single pharmaceutical composition. See *In re Kerkhoven* (MPEP § 2144.06(II)).

16. The combination of Roberts and Morrow, May, and Douthwaite do not teach particular salts of indomethacin, selenium or bismuth, or whether the composition could cross the blood-brain barrier. Berge, et al., teach a variety of FDA-approved anions and note that many of the salts of Claim 69 and 86 are commonly used in pharmaceutical formulations. See Office Action mailed on 01/14/2009. Wilkinson teaches that the blood-brain barrier restricts entry of drugs to the CNS due to physiology of the brain capillary endothelial cells and provides guidance on how to overcome the blood-brain barrier. See Office Action mailed on 01/14/2009.

17. Virtually all pharmaceutical compositions comprise excipients in addition to the active agents that are utilized to generate a pharmaceutical dosage formulation with desired properties, including stability, solubility, buffers, and sweeteners. Thus, the limitiations of instant claim 79 are *prima facie* obvious.

18. For the above reasons, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine indomethacin with at least one of gold, bismuth, or selenium, to utilize salts of these compounds or elements, and to generate a composition that can cross the blood-brain barrier.

Conclusion

19. Claims 66, 69, and 74-86 are rejected.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL ZAREK whose telephone number is (571)270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Paul Zarek/
Examiner, Art Unit 1628